

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1(Previously presented). A conjugate of (1) at least one therapeutic agent for joint diseases and (2) hyaluronic acid, a hyaluronic acid derivative or a salt thereof, wherein said at least one therapeutic agent for joint diseases covalently binds to a carboxyl group of hyaluronic acid, the hyaluronic acid derivative or the salt thereof via a spacer.

Claim 2 (Cancelled).

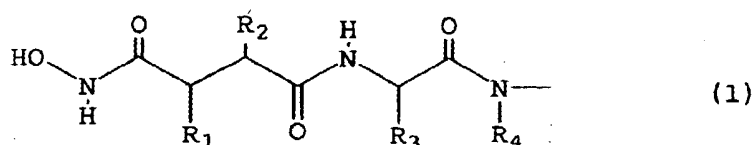
3(Previously presented). The conjugate of claim 1, wherein the therapeutic agent for joint diseases is a matrix metalloprotease inhibitor.

Claim 4 (Cancelled).

5(Previously presented). The conjugate of claim 3, wherein the weight ratio of the matrix metalloprotease inhibitor to the entire conjugate is 0.01 to 50%.

6(Previously presented). The conjugate of claim 3, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue.

7(Previously presented). The conjugate of claim 3, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue represented by the general formula (1):



wherein

R₁ is a hydrogen atom, a hydroxyl group or a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R₂ is a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R₃ is a straight chain or branched alkyl group having 1 to 8 carbon atoms which may be substituted with a cycloalkyl group, an aryl group or a heterocyclic group; and

R₄ is a hydrogen atom or an alkyl group having 1 to 4 carbon atoms.

8(Previously presented). The conjugate of claim 1, wherein the spacer is represented by the general formula (2):



wherein

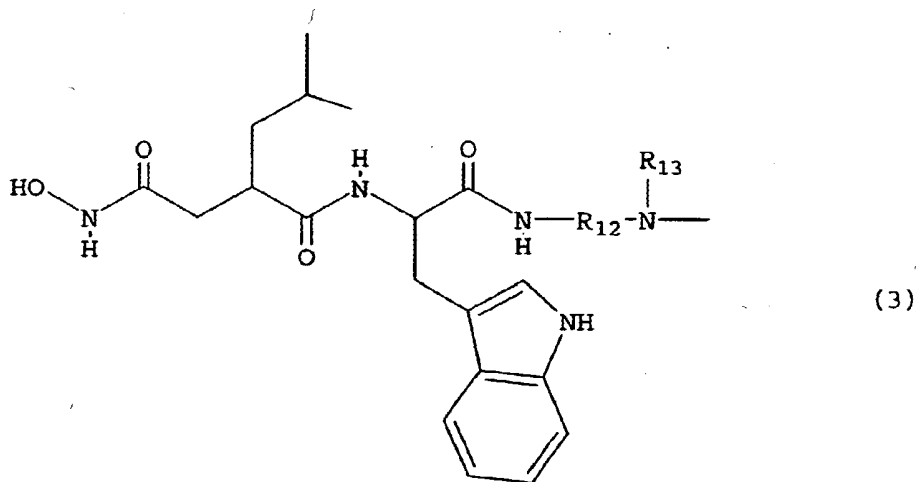
R₅ is a straight-chain or branched-chain alkylene group having 1 to 8 carbon atoms;

R_6 is an oxygen atom or a methylene or imino group which may be substituted with a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms;

R_7 is a straight-chain or branched-chain alkylene group having 1 to 10 carbon atoms into which one to three oxygen atoms may be inserted; and

R_8 is an oxygen atom, a sulfur atom or NR_9 , wherein R_9 is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

9(Previously presented). The conjugate of claim 3, wherein the matrix metalloprotease inhibitor and the spacer constitute a moiety represented by the general formula (3):



wherein

R_{12} is a straight-chain or branched-chain alkylene group having 2 to 23 carbon atoms into which one imino group and/or one to four oxygen atoms may be inserted; and

R₁₃ is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

10(Previously presented). The conjugate of claim 3, wherein the matrix metalloprotease inhibitor in the form of a conjugate with hyaluronic acid, a hyaluronic acid derivative or a salt thereof inhibits a matrix metalloprotease *in situ*.

11(Previously presented). A method for preparing the conjugate of claim 1 comprising binding a site of the therapeutic agent for joint diseases that does not affect the activity of the agent to a carboxyl group, a hydroxyl group or a functional group at the reducing end of hyaluronic acid, a hyaluronic acid derivative or a salt thereof by direct chemical reaction or via a spacer.

12(Currently amended). A pharmaceutical composition comprising the conjugate of any one of claims 1, 3, 5-10, [[18-21]] 18, 19, 23 and 24 and a pharmaceutically acceptable diluent.

Claims 13-16 (Cancelled).

17(Currently amended). A method for treating a patient having a joint disease comprising administering a pharmaceutical composition containing a pharmaceutically effective amount of the

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conjugate of any one of claims 1, 3, 5-10, ~~[[18-21]]~~ 18, 19, 23
and 24 as the effective ingredient to the patient.

18(Previously presented). The conjugate of claim 1,
wherein the therapeutic agent for joint diseases is selected from
the group consisting of a cyclooxygenase 2 inhibitor, an
antirheumatic agent and a matrix metalloprotease inhibitor.

19(Currently amended). The conjugate of claim
1, wherein the ~~spacer bond~~ between ~~at least one therapeutic agent~~
~~for joint diseases~~ said spacer and said hyaluronic acid, ~~a~~
~~hyaluronic acid~~ or derivative or ~~[[a]]~~ salt thereof is selected
from the group consisting of an amide bond, an ether bond and a
sulfide bond.

Claims 20 and 21 (Cancelled).

22(Previously presented). A method of treating a joint
disease in a patient in need thereof, comprising administering a
pharmaceutical composition to said patient in an amount
sufficient for said treatment, wherein said pharmaceutical
composition comprises a conjugate in accordance with claim 1.

23(Previously presented). The conjugate of claim 1,
wherein component (1) is a single therapeutic agent for joint
disease.

24(Previously presented). The conjugate of claim 1,
wherein component (2) is hyaluronic acid or a salt thereof.

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25(Previously presented). The method of claim 17,
wherein the joint disease is selected from the group consisting
of osteoarthritis, rheumatoid arthritis, and scapulohumeral
periarthrititis.